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Research Article

COMPARISON OF ARTERIOVENOUS FISTULAE HAVING BLOOD FLOW EQUALTO AND HIGHER THAN 800 ML/MIN AS REGARDS CLINICAL AND LABORATORY PARAMETERS

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ABSTRACT

We have observed that the lower limit of arteriovenous fistula blood flow accounting for 600 ml / mn as stated by KDOQI guidelines was not enough for performing adequate dialysis, at least in our patients. We had to prove our hypothesis through performing this study. Fifty patients on prevalent hemodialysis were included within our study. 12 patients formed low flow group I, 18 patients constituted moderate flow group II, and 20 patients formed high flow group III. Complete physical examination, including clinical fistula examination for patency, were performed for all patients. Laboratory tests performed for all patients included: URR %, serum calcium, serum phosphorus, calcium – phosphorus product, serum albumin, hemoglobin, serum Iron, serum ferritin, TIBC, TSAT %, Kt / V, serum creatinine, together with blood urea before and after HD session. Fistula blood flow and static venous pressure were determined by Doppler ultrasound. Fistulogram was performed to confirm the fistula stenosis site, whenever detected by Doppler. Mineral bone profile markers, Iron profile markers, together with malnutrition – inflammation complex indicators, were all in favour of moderate and high flow groups, mainly the moderate flow group II due to the presence of much less occurrence of complications than the other groups. We have to try to perform arteriovenous fistulae for ESRD patients needing regular dialysis, in such a way that fistula blood flow is above 800 ml / min, and it is better to be within the range of 801 – 1600 ml / min.

INTRODUCTION

Vascular access problems are a daily occurrence in hemodialysis units. Loss of patency of the vascular access limits hemodialysis delivery and may result in underdialysis that leads to increased morbidity and mortality. Despite the known superiority of autogenous fistulae over grafts, autogenous fistulae also suffer from frequent development of stenosis and subsequent thrombosis. (*Centrao and Turmel – Rodrigues, 2013*).

Dialysis delivery should be adequate not only to improve the quality of life, but also to prolong survival. The quality of life when adjusted for life expectancy has defined a Kt / V of 1.3 as the optimal cost – effective dialysis. An ideal access delivers a blood flow rate to the dialyzer that is adequate for the dialysis prescription, has a long use - life and a low rate of complications including infection, stenosis, thrombosis, aneurysm and limb ischemia. Working fistula must have a blood flow adequate to support dialysis which equates to a blood flow greater than 600 ml / mn. *(Ahmed Samy et al., 2016)*.

Vascular access guidelines recommend routine screening for the timely detection of stenosis using noninvasive methods, including clinical assessment (monitoring) and device-based surveillance relying on access blood flow (Qa) and static intra-access pressure (sVPR, static venous pressure ratio) measurements and duplex ultrasound (DU). (*Tessitore et al., 2014*).

Large scale studies have shown the existence of a consistent relationship between bone mineral disease indices and morbidity and death within prevalent hemodialysis patients. (*Norris et al., 1985; Block et al, 1998; Block et al., 2004, Kestenbaum et al., 2005; Slinin et al., 2005*).

Anemia contributes markedly to morbidity in patients with chronic renal insufficiency treated with hemodialysis. (*Erslev, 1991; Nissenson, 1991; Rao et al., 2016*).

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The medical management of maintenance hemodialysis patients by clinicians is usually based on repeated measurements of blood tests. *(KalantarZadeh et al., 2006)*.

PATIENTS AND METHODS

This is a cross – sectional study. It was conducted at dialysis units, Ain Shams University Hospitals. Fifty patients have participated in this study.

Patients enrolled in this study had a native arteriovenous fistula and were on prevalent hemodialysis. All patients were above 18 years, receiving regular hemodialysis sessions thrice weekly, each session lasting for 4 hours each. Patients were using high or low flux dialyzers, and bicarbonate or acetate dialysate solution, and receiving a dose of Erythropoietin of 4000 IU / week.

We excluded from our study patients having vasculitis as ESRD etiology, patients having Diabetes Mellitus or peripheral vascular disease, patients having antiphospholipid and anticardiolipin syndrome, and patients having thrombotic episodes due to Protein C, Protein S, or Antithrombin III deficiency.

Our patients were divided into 3 groups according to native arteriovenous blood flow estimated by Doppler ultrasound

Low Flow Group I: included 12 patients having estimated arteriovenous fistula blood flow less than 800 ml / min.

Moderate Flow Group II: comprised 18 patients having estimated arteriovenous fistula blood flow from 801 to 1600 ml / min.

High Flow Group III: was formed of 20 patients having estimated arteriovenous fistula blood flow greater than 1600 ml / min.

For all patients included within the study, complete physical examination was performed. Clinical examination of arteriovenousfistula included the following: Arm swelling (+ = hand swelling, ++ = hand and forearm swelling, +++ = hand, forearm, and arm swelling), collaterals (+ ve = present, - ve = absent), difficult cannulation (+ ve = present, - ve = absent), prolonged bleeding time after needles removal (+ ve> 3 minutes, - ve≤ 3 minutes), signs of inflammation (+ ve = present, - ve = absent, including cardinal signs of inflammation), Aneurysm / pseudoaneurysmfoemation (+ ve = present, - ve = absent) , impending rupture signs (+ ve = present, - ve = absent) , and lastly thrill and pulse at fistula site (+ ve = present, - ve = absent).

Augmentation Test: Is performed to evaluate inflow stenosis within arteriovenous fistula, (+ ve = present in patent arteriovenous fistula, - ve = absent in stenosis). Place your fingers on the out-going vein, feel the pulse, press down until no blood is flowing through the access. Keep your finger on the vein and feel for the pulse on the lower part of the access. The thrill should become a strong pulsation (+ ve), if not, there may be inflow obstruction.*(Asif et al., 2007)*.

Hand Elevation Test: Collapse of the post- stenotic venous segment and persisting congestion of the pre – stenotic segment, is considered as indicating a positive test.

Dialysis Data: Average pump speed used during dialysis was 300 to 400 ml / min, and static venous pressure considered within accepted range was from 100 – 200 mm/ Hg, with an average of 150 mm / Hg, (accepted as normal).

Laboratory Parameters: These included serum creatinine before and after hemodialysis session (in mg /dl), blood urea before and after session (in mg / dl), URR % = [(Urea before – Urea after)/Urea before], serum calcium before session (in mg /dl), serum phosphorus before session (in mg / dl), calcium – phosphorus product (in mg^2 / dl^2), Parathyroid hormone (PTH) before session (in pg / ml), serum albumin before session (in g / dl), hemoglobin before session (in g / dl), serum iron before session (in mcg/dl), serum ferritin before session (in ng/dl), TIBC before session (in mcg / dl), TSAT % before session, and KT / V (our minimum = 1.2).

Doppler Ultrasound Evaluation of Fistula : To estimate fistula blood flow volume (ideally ranging from 600 ml / min to 2000 ml / min), to detect whether thrombosis is present (+ ve) or absent (- ve), and to detect site of stenosis of the vein involved within arterio-venous fistula (whether above fistula or within fistula itself), and the latter item was confirmed by fistulogram performance (after patient 's consent).We also have used Doppler to measure static venous pressure (being the sustained type of pressure exerted upon venous wall in arteriovenous fistula and equivalent to the vascular tone existing during diastolic episode of cardiac cycle, within normal vasculature without arteriovenous shunt

We used the Doppler Scanner linear probe with minimum frequencies of 7 MHz for the B – mode examination and 5 MHz for the Doppler study and calculation of arteriovenous fistula flow volume according to (*Wiese and Nonnast – Daniel, 2004)*. The evaluation procedure was performed according to *Malvorh, 2003*. The apparatus used is M5 color Doppler ultrasound by Mindray Co., China.

Fistulography: This procedure was performed in cases found to have stenosis by Doppler evaluation. Fistulography was done using an apparatus named BV pulsera mobile C arm, by Philips Co., USA.

Statistical Methods

Data management and statistical analysis were performed using the Statistical Package for Social Sciences (SPSS) version 21. Numerical data were summarized using means and standard deviations or medians and ranges. Categorical data were summarized as percentages. Data will be explored for normality using Kolmogrov-Smirnov test and Shapiro-Wilk test. For categorical variables, differences were analyzed with χ^2 (chi square) test and Fisher's exact test when appropriate.

Differences among the three groups (low flow group I, moderate flow group II, and high flow group III) were analyzed with Univariate ANOVA and Bonferroni post hoc test or Kruskal Wallis test (nonparametric analogue for ANOVA) followed by Mann Whiteny test. Correlations among different variables were determined by using Pearson's test. All p-values are two-sided. P-values ≤ 0.05 were considered significant. P< 0.01 was considered highly significant. P > 0.05 was considered nonsignificant.

RESULTS

In our study, low flow group I showed an age mean value of 53.8 ± 7.9 years (ranging from 40 – 68 years), moderate flow group II had a mean age of 46.3 ± 13.0 years (ranging from 24 - 68 years), and within high flow group III, it was 46 .6 ± 14.0 years (ranging from 19 – 71 years).

As regards etiology of ESRD, 19 out of the 50 patients included within the study (38.0 %) had hypertension, 10 patients out of 50 (20 %) had unknown etiology, 3 patients out of 50 (6 %) had the cardio – renal syndrome. The following pathological states existed each within 2 patients out of 50 (4 %): Analgesic abuse, lupus nephritis, pyelonephritis, and renal atrophy. Each of amyloidosis, congenital ureteric aplasia, diabetes mellitus, hypertension accompanied by back pressure changes within kidneys, hypertension accompanied by renal atrophy, ischemic ATN, kidney congenital deformity, polycystic kidney disease, post – streptococcal glomerulonephritis, and toxic ATN, existed only within 1 patient out of 50 (2 %).

Table 1 Comparison of low flow group I, moderate flow group II, and high flow group III as regards factors affecting arteriovenous blood flow and static venous pressure: Arm swelling, difficult cannulation, prolonged bleeding after needle withdrawal, signs of inflammation and infection, aneurysm / pseudoaneurysm formation, impending rupture, signs of vascular steal phenomenon, thrill and pulse within native arteriovenous fistula, Augmentation test, and Hand Elevation test.

		GROUP 1		GROUP II		GROUP III		P VALUE
		NO	%	NO	%	NO	%	
Arm Swelling	NO	8	66.7	13	68.4	17	89.5	0.215
	YES	4	33.3	6	31.6	2	10.5	
Difficult Cannulation	NO	8	66.7	17	89.5	15	78.9	0.299
	YES	4	33.3	2	10,5	4	21.1	
Prolonged Bleeding	NO	9	75.0	16	84.2	14	73.7	0.706
	YES	3	25.0	3	15.8	5	26.3	
SIGNS OF INFL. & INFECTION	NO	11	91.7	16	84.2	19	100.0	0.2
	YES	1	8.3	3	15.8	0	0.0	
ANEURYSM/ PSEUDO – ANEURYSM	NO	8	66.7	2	10.5	2	10.5	0.001
	YES	4	33.3	17	89.5*	17	89.5*	
IMPENDING RUPTURE	NO	11	91.7	17	89.5	19	100.0	0.364
	YES	1	8.3.0	2	10.5	0	0.0	
SIGNS OF STEAL	NO	9	75.0	14	73.7	14	73.7	0.996
	YES	3	25.0	5	26.3	5	26.3	
THRILL	NO	1	8.3	0	0.0	0	0.0	0.199
	YES	11	91.7	19	100	19	100.0	
Augmentation Test	+ VE	10	83.3	19	100.0&	19	100.0 &0.037	
	- VE	2	16.7	0	0.0	0	0.0	
Hand Elevation test	- VE	10	83.3	18	94.7	19	100.0	0.161
	+ VE	2	16.7	1	5.3	0	0.0	

(&, *) indicates the groups having statistical significance with group I
Chi – square test, Fischer exact test, and Kruskal Wallis followed by Mann Whitney test were used
Pulse was removed from table as it was constantly present in the same pattern within the 3 studied groups

There were 6 male and 6 female patients within low flow group I, with a male / female percent ratio of 50 / 50. Within moderate flow group II, we had 12 male and 7 female patients with a male / female percent ratio of 63.2 / 36. 8. The high flow group III was constituted of 11 male and 8 female patients, with a male / female percent ratio of 57.9 / 42.1.

The presence of general medical disease within past history affected 9 patients out of 12 (81.8 %) within low flow group I, while this percentage was much decreased within both moderate flow group II having 11 patients out of 19 (57.9 %), and high flow group III having 11 patients out of 19 (57.9 %). 8 patients out of 19 (42.1 %) included within high flow group III, were completely free until dialysis therapy initiation. Within moderate flow group II, only 5 patients out of 19 (26.3 %) were free before dialysis initiation, while none of the patients (0.0 %) included within low flow group I was completely free before dialysis.

According to medical record data, local inflammatory changes within arteriovenous fistula were present only in 2 patients out of 12 (18.2 %) within low flow group I. These changes existed within only 3 patients out of 19 (15.8 %) included in moderate flow group II. None of the high flow group III patients has shown such local pathological changes (0.0 %).

Table 2 Comparison of low flow group I, moderate flow group II, and high flow group III as regards Type of arteriovenous fistula, duration of functioning arteriovenous fistula (AVF) now, arteriovenous fistula thrombosis, stenosis, and Collection of blood around venous side of arteriovenous fistula.

		Group I		Group II		Group III		P value
		No	%	No	%	No	%	
TYPE OF AVF	Brachio – Cephalic	6	50.0	14	73.7	14	73.7	
	Radio – Cephalic	6	50.0	5	26.3	5	26.3	0.309
Thrombosis	- VE	9	75.0	19	100.0&	19	100.0&	0.006
	+ VE	3	25.0	0	0.0	0	0.0	
Stenosis	- VE	9	75.0	19	100.0$	18	94.7$	0.038
	+ VE	3	25.0	0	0.0	1	5.2	
Collection	- VE	11	91.7	18	94.7	19	100.0	0.483
	+ VE	1	8.3	1	5.3	0	0	

(&, $) indicate the groups having statistically significant difference with group I
Chi – square test, Fisher exact test, and Kruskal Wallis followed by Mann whitney test were used

Table 3 Comparison of low flow group I, moderate flow group 2, and high flow group 3 as regards: areriovenous fistula blood flow (ml / min), static venous pressure (mmHg), URR % , serum calcium (mg / dl), serum phosphorus (mg / dl), calcium – phosphorus product (Ca x Ph, mg 2/ dl2), serum albumin (g / dl), serum Hb (g /dl), serum iron (mcg / dl), serum ferritin (ng / dl), serum TIBC (mcg / dl), and TSAT %.

	GROUP I		GROUP II		GROUP III		P value
	Mean	SD	Mean	SD	Mean	SD	
AVF blood flow	573.8	200.6	1160	229	2756	929.3	< 0.001`
Static v. pressure	164.2	27.8	151.1	4.6	150	0	0.016
URR %	57.1	11.6	63.1	10.4	62.5	15.2	0.408
Calcium	8.6	1.2	8.7	1.3	8.8	1.2	0.957
Phosphorus	4.9	1.5	4.3	2.4	4	2.3	0.542
Ca x Ph	40.96	10.33	36	20.47	34.26	18.76	0.593
Albumin	4.1	1.9	3.9	0.6	3.9	0.3	0.834
Hb	10.5	2	11.7	2.5	11	2.1	0.336
Iron	54.4	34.4	62.2	30.3	60.2	33.4	0.806
Ferritin	433	54.7	836 $^{\$}\pm$ 76.5		847 $^{\$}\pm$ 55.8		0.017
TIBC	274.5	75.1	217.7 $^{*}\pm$ 65.4		217.2 $^{*}\pm$ 52.2		0.032
TSAT %	20	13.9	32.4	22.2	28.7	17.2	0.213

($, *): indicate the groups having statistically significant difference with group I
One way Anova followed by Bonferroni post hoc test were used. Analysis was repeated by non – parametric test to ensure robustness of the results.

Table 4 Comparison of low flow group I, moderate flow group II, and high flow group III as regards urea before session, urea after session, weght before session, weight after session, and Kt / V.

	Group I	Group II	Group III	P value 1
	Mean ± SD	Mean ± SD	Mean ± SD	
Urea beforesession	86.2 ± 44.8	83.6 ± 45.3	92.7 ± 43.2	0.812
Urea aftersession	36.3 ± 18.4	29.1 ± 12.4	31.9 ± 17.3	0.48
P value 2	< 0.001	< 0.001	< 0.001	
Weight before session	84.7 ± 15.3	74.1 ± 17	76.9 ± 11.7	0.156
Weight after session	82.5 ± 14.7	72.1 ± 16.7	75 ± 11.6	0.15
P value 2	< 0.001	< 0.001	< 0.001	
Kt / V	1.01 ± 0.2	1.22 ± 0.3	1.2 ± 0.3	0.113

P value 1: for comparing between groups
P value 2: for comparing before and after session values within the same group

The duration of hemodialysis duration median value was 3.3 years (ranging from 0.6 – 11), within low flow group I, 9 years (ranging from 1-22) within moderate flow group II, and 8 years (ranging from 0.5 – 22) within high flow group III.

The median value of duration of functioning fistula was 2 years within low flow group I (ranging from 0.5 – 7 years), 9 years within moderate flow group II (ranging from 0.7-22 years), and 5 years within high flow group III (ranging from 0.5 – 20 years).

As the number of previously failed native fistula, wit within the low flow group I, 3 patients out of 12 (25 %) had one previous event of fistula failure, and only 1 patient out of 12 (8.33 %), has suffered twice from previous fistula failure. Within moderate flow group II, 3 patients out of 19 (15. 79 %) had previously experienced previous two events of failed fistula, while only one patient out of 19 (5.26 %) within the same group, had previously failed fistula event for 3 times, and only patient out of 19 (5.26 %) has got previous fistula failure for 4 times. Within high flow group III, 4 patients out of 19 (21.05 %) have experienced previous fistula failure once, while 1 patient out of 19 (5.26 %) has previous fistula failure twice, and only 1 patient out of 19 (5.26 %) had a history of previous fistula failure for three times.

The mean difference value of blood urea before and after session was- 49.9 mg/dl within low flow group I (95 % CI = 31.7–68.1, % reduction= -57.9, P < 0.001), in moderate III it was- 60.8 mg/ dl (95 % CI = 45.2–76.4, % reduction = - 65.6, P < 0.001).

The mean difference value of weight before and after session was - 2.1 Kg within low flow group I (95 % CI = 1.5 – 2.8, % reduction= - 2.6, P < 0.001), in moderate flow group II it was - 2.1 Kg (95 % CI= 1.6 – 2.5, % reduction = - 2.7, P < 0.001), and within high flow group III it was - 1.9 Kg (95 % CI = 1.5 – 2.3, % reduction= -2,5, P < 0.00).

Median value of Parathyroid hormone was 440 pg /ml within low flow group I (ranging from 132 - 3408 pg / ml), 461 pg / ml within moderate flow group II (ranging from 38 – 3606 pg / ml), and 563 pg/ ml with high flow group III (ranging from 118 – 1613 pg / ml), with no statistically significant difference found between the three groups, (P = 0.820).

DISCUSSION

The aim of dialysis is to decrease morbidity, increase the quality of life and prolong life span. *(Port et al., 2002)*. To achieve this, dialysis must be performed effectively .*(Sehgal et al., 2001)*. The inadequate dose of dialysis increases the duration of hospitalization and the overall cost of care. *(DiGiulio et al., 1998; Ahmed Samy et al., 2016)*.

The European Best Practice Guidelines 2004, (*Locatelli et al., 2004; Horl et al., 2007*), and Italian Guidelines 2003, (*Triolo etal., 2003; Canavese et al., 2007*), stated the following ranges as accepted: Hemoglobin level ≥ 11 to ≤ 12 g / dl, Kt / V > 1.2 To 2.0 for non – diabetic patients, Serum Iron 60 to 160 mcg / dl, Serum Ferritin 30 to 400

mcg / l, and Transferrin saturation percentage > 25 to 50 %.

The National Kidney Foundation (NKF) issued the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines for Vascular Access in an effort to improve patient survival and quality of life, reduce morbidity, and increase the efficiency of care. A working fistula must have a blood flow adequate to support dialysis which is usually equal to a blood flow greater than 600 ml / mn. *(National Kidney Foundation, 2001; Ahmed Samy et al., 2016).*

Access stenosis or thrombosis is a costly threat to patency in association with significant morbidity to the patient. *(Schwab et al., 1989; Gibbsonand Dzu, 1994; Ahmed Samy et al., 2016).*

In our study, age was non – significantly higher in low flow group I patients, as compared to each of moderate flow group II patients and high flow group III patients, (P = 0.216). This means that age didn 't directly affect arteriovevenous fistula blood flow and static venous pressure and all our results.

Hemodialysis duration was significantly higher within each of moderate flow group II patients (P = 0.028), and high flow group III patients (P = 0.028), as compared to low flow group I patients. Both groups having predominant brachiocephalic fistula type, and also predominant male gender.

The highest number of patients who have been subjected to native access failure before, was present within high flow group III, against what was expected, may be due to the injurious effect of high blood flow on arteriovenous fistula ultrastructure, including hemodynamic and shear stress effects, moderate flow group II was affected to a less extent, and low flow group I was the least affected.

Duration of functioning fistula was significantly higher within moderate flow group II and high flow group III, as compared to low flow group I. (P = 0.003, and P = 0.027, respectively), with no statistically significant difference between group II and group III.

The presence of higher percentage of patients having brachio – cephalic fistula (> 50 % of patients), explained the presence of higher fistula blood flow within moderate flow group II and high flow group III. But this higher percentage of brachio – cephalic fistulae didn 't show an evident statistically significant difference between these two groups and low flow group I, comprising only 50 % of patients having brachio – cephalic fitulae, (P = 0.309). In spite of this, *Miller et al., 1999*, reported that upper arm fistulae had higher adequacy rates than the forearm fistulae, (P = 0.012), especially so in women and elderly.

Augmentation test, reflecting free arteriovenous fistula flow, was negative (denoting flow obstruction) in a significantly higher number of patients within low flow group I, as compared to moderate flow group II and high flow group III (P = 0.037). Hand elevation test was positive (denoting stenosis) within a higher number of patients within low flow group I, in a non-significant way than the other 2 groups and there was no much difference as regards the results of the two previously mentioned tests , within group II and group III, as compared to each other. These tests have revealed an advantage of the relatively adequate free blood flow within moderate and high blood flow fistulae, and inspite of this Low flow group I had the highest percentage of patients showing positive vascular steel phenomenon, as compared to the other two groups, in a non – significant way.

Low flow group I had also the significant higher rate of shunt thrombosis than each of moderate flow group II and high flow group III (P = 0.006). This also applies to stenosis percentage rate, which was significantly higher within low flow group I as compared to each of moderate flow group II and high flow group III.(P = 0.038).

Basile et al., 2004, have reported that the value of vascular access flow rate, identified as a predictor of access failure, was <700 ml / min, with an 88.9 % sensitivity and 68.6 % specifity. 79.2 % of patients who had arteriovenous fistulae patent all through the 4 years of the study, had a blood flow rate $\geq$ 900 ml / min, while only 20.8 % of them had an arteriovenous fistula blood flow rate consistently $\leq$ 500 ml / min. They have shown that blood flow rate of 700 ml / min was a cut off point for fistula stenosis and thrombosis.

In hemodialysis patients with an arteriovenous fistula, access failure is primarily due to fistula stenosis, which predisposes to thrombosis and subsequent access loss*.(Mattana et al., 1997; Ahmed Samy et al., 2016).*

The stenosis site within the 3 obstructed cases belonging to low flow group I, was at the fistula itself as documented by both Doppler assessment and also by fistulogram. The stenosis site within the stenosed case belonging to group III, was above fistula level by about 3 cm as detected by both Doppler examination and fistulogram.

The previously mentioned low flow group I has shown the highest static venous pressure value as compared to moderate flow group II (P = 0.038), and high flow group III (P = 0.022). The fistula static venous pressure was nearly the same within moderate flow group II and high flow group III without significant difference between them (P = 1). Static venous pressure has shown a highly significant inverse correlation to arteriovenous fistula blood flow within low flow group I (R = - 0.893, P < 0.001), and a significant positive relationship to fistula blood flow within moderate flow group II, (R = 0.465, P = 0.045).This relationship didn 't exist within high flow group III, as static venous pressure was constant at accepted range within this group, without any problems.

The statistically significant difference between low flow group I as regards blood flow and static venous pressure as compared to both moderate flow group II and high flow group III, didn 't have any obvious significant impact upon URR %, serum calcium, serum phosphorus, calcium – phosphorus product, PTH level, and serum albumin, inspite of the existence of slight non–significant differences within values of these parameters within low flow group I as compared to the other two groups. Inspite of this, within moderate flow group II, blood urea level

has constantly shown the lowest mean level before and after session. Urea before and after session have shown a significant positive correlation to each other within low flow group I ($R = 0.925$, $P < 0.001$), and moderate flow group II ($R = 0.758$, $P < 0.001$), and this relationship didn 't exist within high flow group III.

The mean difference value of serum creatinine was non - significantly higher within low flow group I as compared to the other 2 groups ($P > 0.05$). The mean difference value of urea before and after session within each of the studied 3 groups, has shown the lowest value within low flow group I, and it was moderate within moderate flow group II. The highest value was found within high flow group III. Inspite of this, on comparing the mean difference of the three groups to each other, we didn 't find a statistically significant difference between them ($P > 0.05$). On performing Pearson correlation test, we found within high flow group III significant positive relationship between mean value of urea after session and each of phosphorus ($R = 0.486$, $P = 0.035$), and calcium – phosphorus product ($R = 0.544$, $P = 0.016$).

URR % has shown the least mean value within low flow group I , in a non – significant way as compared to the other 2 groups , who both had very close mean value ranges of URR % . URR % has shown a highly significant inverse relationship to mean level of urea after session within high flow group III ($R = 0.640$, $P = 0.003$). This quite logical relationship didn 't exist within low and moderate flow groups, may be because of less clearance of uremic toxins including urea within these 2 groups On adding and substracting and SD values of serum calcium, we found that it was around the accepted normal range within the three studied groups. Serum calcium had non - significantly a lesser mean value within low flow group I, as compared to the other 2 groups.

Ahmed Samy et al., 2016, have found in their study a positive correlation between the inflammatory marker tumor necrosis factor - alpha and serum calcium. We have found in our study a significant positive correlation between calcium and serum albumin within moderate flow group II ($R = 0.675$, $p = 0.002$).

Serum phosphorus and calcium – phosphorus product had non – significantly higher values within low flow group I, as compared to the other 2 groups. These findings were not in favour of the low flow group I. Within high flow group III, URR % has shown a highly significant inverse correlation to each of serum phosphorus ($R = - 0.782$, $P < 0.001$), and calcium - phosphorus product ($R = - 0.764$, $P < 0.001$). These findings were confirmed by a significant positive correlation found by *Kalantar - Zadeh et al., 2006*, between serum phosphorus and serum creatinine, ($P < 0.01$).

Only within moderate flow group II, Kt / V also has shown a significant inverse correlation to each of serum phosphorus ($R = - 0.462$, $P = 0.047$), and calcium- phosphorus product ($R = - 0.518$, $P = 0.023$).

PTH was correlated to Calcium - phosphorus product in a significant positive relationship within high flow group III ($R = 0.476$, $P = 0.04$). This relationship didn 't exist within low and moderate flow groups.

Inspite that serum calcium and phosphorus values out of accepted ranges by KDOQI was associated with death risk, researchers couldn 't find a direct relationship between the parathyroid hormone level considered as a uremic toxin and death risk, due to the existence of inter-related factors. (*Kalantar – Zadeh et al, 2006*).

Surprisingly, serum albumin level had higher mean level within low flow group I than the other 2 groups, in a non – significant way. On adding and substracting SD to and from mean serum albumin value, we find that it ranges from (2.2 – 6 gm / dl) within low flow group I, ranging from hypoalbuminemia to hyperalbuminemia (denoting albumin level instability and unpredictable state), (3.3 – 4.5 gm / dl) within moderate flow group II and (3.3 - 4.2 gm / dl) within high flow group III, being nearer to normal within the last two groups. This is definitely against low flow group. Fistula blood flow has shown a significant inverse correlation to serum albumin within low flow group I ($R = - 0.590$, $P = 0.043$), and this relationship did not exist within the other 2 groups and this needs to be further studied and explained. *Ahmed Samy et al, 2016*, has reported that albumin has shown a consistent inverse correlation to inflammatory markers such as tumor necrosis factor b – alpha, and this was previously confirmed within *Undurti N. Das, 2015*. Also, a significant positive relationship existed between mean level of urea after session and serum albumin within low flow group I ($R = 0.708$, $P = 0.01$), and moderate flow group II ($R = 0.510$, $P = 0.026$), but not within high flow group III. From this, we could deduce that there was some relationship between arteriovenous fistula adequacy, its blood flow, and serum albumin . Inspite of this, *Miller et al, 1999*, have shown in their study that there was no relationship between arteriovenous fistula adequacy and serum albumin.

Weight before and weight after session have constantly shown the highest mean values within low flow group I , but in a non – significant way, while these two parameters have constantly shown the lowest mean levels within moderate flow group II, but also in a non – significant pattern .The highest percent reduction in weight was found within moderate flow group II, in a non – significant way as compared to the other two groups, reflecting a better BMI, better quality of life, more compliance to daily activities and dialysis procedure, together with less less ability to adapt to morbidity. *Miller et al., 1999*, has shown that within overweight patients having BMI> 27 Kg/ m^2, arteriovenous fistula adequacy is much decreased than non – overweight patients, ($P = 0.07$).

Kt / V mean value within low flow group I was < 1.2, and the highest mean value of Kt / V existed within moderate flow group II, but in a statistically non – significant way. Within high flow group III, mean value of urea after session has shown a significant inverse correlation to Kt / V ($R = - 0.517$, $P = 0.024$). This relationship didn 't exist

within low and moderate flow groups, and this finding was in favour of the high flow group. A highly significant positive relationship existed between URR % and Kt / V within low flow group I (R = 0.825, P = 0.001), moderate flow group II (R = 0.987, P < 0.001), and high flow group III (R = 0.580, P = 0.009). Only within high flow group III, serum albumin has shown a significant positive relationship to Kt / V (R = 0.549, P = 0.048). Only within high flow group III, PTH has shown a significant inverse correlation to Kt / V only within high flow group III (R = - 0.473, P = 0.041). Inspite of this, *Miller et al., 1999*, have shown in their study, that there was no relationship between arteriovenous fistula adequacy and PTH.

Hemoglobin, serum Iron, and TSAT % have shown the highest mean values within moderate flow group II, and the lowest mean values within low flow group I, in a statistically non – significant pattern.

Serum ferritin was significantly lower within low flow group I as compared to the other 2 groups. (P = 0.017). Only within moderate flow group II, Iron has shown a significant positive relationship to hemoglobin level (R = 0.493, P = 0.032), this could mean that within this flow range patients had benefit from iron intake to raise their hemoglobin, while we could not assure the presence of this relationship within the low and high flow groups whatever the right explanation would be. Only within low flow group I, a significant positive relationship existed between Kt / V and hemoglobin (R = 0.807, P = 0.002), which explained the lower hemoglobin range existing within this group. *Movilli et al., 2001; Movilli et al. , 2003; and Locatelli et al., 2006*, have reported a link between dialysis adequacy and erythropoiesis.

Hemodialysis duration has shown a significant positive relationship to serum ferritin within high flow group III (R = 0.571 , P = 0.011), this relationship didn ' t exist within low and moderate flow groups. Serum ferritin has shown a significant positive relationship to serum Iron only within low flow group I (R = 0.799, P = 0.002) and moderate flow group II (R = 0.661, p = 0.002), but this relationship didn 't exist within the high flow group. Only within moderate flow group II, Ferritin has shown a highly significant inverse relationship to TIBC (R = 0.741, P < 0.001), and this rational. Serum ferritin has shown a highly significant relationship to TSAT % within both low flow group I (R = 0.835, P = 0.001) and moderate flow group II (R = 0.849, P < 0.001), but not within high flow group . Serum ferritin has been found to have a significant inverse correlation to PTH within moderate flow group II only (R = 0.518, P = 0.023). This represented an important link between PTH and iron stores within uremic patients, and this became very evident within patients having fistula flow ranging from 801 – 1600 ml / mn. *Kalantar – Zadeh et al. , 2009*; and *Gaweda et al., 2010*, have reported that iron deficiency indicated by low levels of ferritin and TSAT is associated with an impaired erythropoiesis. *Gaweda et al., 2010*, reported that impaired erythropoiesis is also present when ferritin is elevated above 500 ng / ml, as malnutrition - inflammation syndrome inhibited erythropoiesis.

Observations have been made relating anemia to marrow fibrosis in patients with uremia who have secondary hyperparathyroidism, as reported by *Urena et al., 1991; and Rao et al., 2016*. Also, according to the same authors, improvement in anemia has been reported after parathyroi – dectomy. A direct inhibitory effect of parathyroid hormone on erythropoiesis was reported in one study conducted by *Gaweda et al., 2010*.

Only within high flow group III, serum calcium has shown a significant positive relationship to ferritin, which is an inflammatory marker (R = 0.485, P = 0.035). Calcium and ferritin are among markers of two major problems we have within dialyzed patients. TIBC also was significantly higher within low flow group I as compared to the other 2 groups. (P = 0.032). This reflects a state of possibly not enough adequate dialysis affecting low flow group I, a malnutrition state due to a much disturbed homeostasis within an internal environment stuffed with uremic toxins, and certainly a decreased sensation of well being and quality of life.

Confirming previous results concerning superiority of moderate and high flow groups, hemodialysis duration showed a significant inverse correlation to TIBC within high flow group III (R = - 0.518, P = 0.023), indicating a better iron profile parameters state within this group .This relationship didn 't exist frankly as such within the other two groups. Inspite of this, moderate flow group II had the best iron profile parameters as a whole, when compared to the other two groups. Within low flow group I, serum albumin showed a highly significant positive relationship to each of serum Iron (R = 0.841, P = 0.001), serum ferritin (R = 0.882, P =0.001), TSAT % (R = 0.831, P = 0.001). These relationships existing only within low flow group having the highest static venous pressure, reflect the impact of an inflammatory rather than a malnutritional state. *Gaweda et al., 2010*, have shown that severe hypoalbuminemia due to malnutrition – inflammation complex, was associated with significant decrement within erythropoietic process. Serum Iron had a highly significant positive relationship to TSAT % within each of low flow group I (R = 0.887, P < 0.001), moderate flow group II (R = 0.864, P < 0.001), and high flow group III (R = 0.885, P < 0.001). Serum transferrin, but not TSAT %, have shown a positive relationship to BMI (P < 0.018) within the study performed by *Soffritti et al., 2009*. PTH has shown a significant positive relationship to TIBC only within moderate flow group II (R = 0.472, P = 0.041).

CONCLUSION

We have on performing an arteriovenous fistula to take our measures to ensure that blood flow within the newly constructed shunt will be above 800 ml / mn and it will be better to be within the moderate range of 801- 1600 ml / mn or above it, as this range has shown in most instances, to be the best blood flow within arterio – venous shunt providing mostly adequate dialysis procedure reflected on both clinical and laboratory parameters, longest fistula survival and the least rate of complications.

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